29 RECEINED 7

JUL 0 5 2001 **TECH CENTER 1600/2900**

• •	16011 CENTER 1600/2900
RAW SEQUENCE LISTING PATENT APPLICATION: US/09/2	DATE: 06/12/2001 97,486 TIME: 13:11:24
Input Set : A:\GJE-30.txt Output Set: N:\CRF3\06122001	of an Agent That Stimulates NO or P.Z.
4 <110> APPLICANT: Martin, John Francis	#1~
5 Yla-Herttuala, Seppo	7-9-01
6 Barker, Stephen George Edward	, , , , , ,
8 <120> TITLE OF INVENTION: Therapeutic Use	of an Agent That Stimulates NO or 7.2.
Prostacyclin Production	
9 and Delivery Device	· ·
11 <130> FILE REFERENCE: GJE-30	
13 <140> CURRENT APPLICATION NUMBER: US 09/2	97,486
C> 14 <141> CURRENT FILING DATE: 2001-05-24	
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17 <151> PRIOR FILING DATE: 1997-11-03	
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20 <151> PRIOR FILING DATE: 1996-11-01	
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46 tac ctc cac cat gcc aag tgg tcc cag gct g	
47 Tyr Leu His His Ala Lys Trp Ser Gln Ala A	
48 20 25	
50 gga ggg cag aat cat cac gaa gtg gtg aag t	
51 Gly Gly Gln Asn His His Glu Val Val Lys P 52 35 40	. 1
52 35 40 54 cgc agc tac tgc cat cca atc gag acc ctg g	45 In gac ato the eag gag 192
55 Arg Ser Tyr Cys His Pro Ile Glu Thr Leu V	3 3 3
56 50 55	60
58 tac cct gat gag atc gag tac atc ttc aag c	
59 Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys P:	
	75 80
62 atg cga tgc ggg ggc tgc tgc aat gac gag g	
63 Met Arg Cys Gly Gly Cys Cys Asn Asp Glu G	
64 85 90	95
66 act gag gag too aac atc acc atg cag att a	g egg ate aaa eet eac 336
67 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile M	et Arg Ile Lys Pro His
68 100 105 .	110
70 caa ggc cag cac ata gga gag atg agc ttc c	a cag cac aac aaa tgt _. 384

RAW SEQUENCE LISTING DATE: 06/12/2001 PATENT APPLICATION: US/09/297,486 TIME: 13:11:24

Input Set : A:\GJE-30.txt

Output Set: N:\CRF3\06122001\1297486.raw

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74 gaa tgc a		aag a	aaa σa		σca	aσa	caa	σaa		t.at.	gac	aaσ	432
75 Glu Cys A	-	_	-	_	-	_		_		_	_	_	
76 130			13					140		012		-1-	
78 ccg agg c	aa '							110					441
79 Pro Arg A	-												
80 145	- 9												
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84 <211> LEN													
85 <212> TYP		: /											
86 <213> ORG		Цото	canio	nc									
88 <400> SEQ			sapre	115									
			on To	n Wall	IIi a	man	Cor	T 011	7 J a	T OU	T 011	T OU	
90 Met Asn P	ne Leu		ser ii	р уат	HIS		ser	Leu	Ата	ьeu		Leu	
91 1		5			01 =	10	21.	Desc	14 a da	7. J	15	<i>α</i> 1	
93 Tyr Leu H		ата і	Lys Tr	p ser		Ата	Ala	Pro	мет		GIU	GIY	
94	· 20				25	_	-1		_	30			
96 Gly Gly G		H1S H	dis GI		val	Lys	Phe	Met		Val	Tyr	GIn	
	35			40		_	•	_	45		_ 7		
99 Arg Ser T	yr Cys	His H			Thr	Leu	Val	_		Phe	GIn	GLu	
100 50	_			55				60		_			
102 Tyr Pro	Asp Glu	Ile		yr Il	e Phe	e Lys			СУЗ	va]	Pro		
103 65 .			70				75					80	
105 Met Arg	Cys Gly	Gly	Cys C	ys Ası	n Asp		_	, Leu	Glu	Суя	val	Pro	
106		85				90					95		
108 Thr Glu	Glu Ser	Asn	Ile T	hr Me	t Glr	11ϵ	e Met	. Arg	Ile	Lys	s Pro	His	
109	100				105					110			
111 Gln Gly	Gln His	Ile	Gly G	lu Met	t Sei	: Phe	e Leu	ιGln	His	Asr	ı Lys	Cys	
112	115			120	0				125	,			
114 Glu Cys	Arg Pro	Lys	Lys A	sp Ar	g Ala	a Arg	g Gln	Glu	Lys	Cys	asp	Lys	
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133 Met Asn													
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136 tac ctc	cac cat	gcc	aag t	gg tco	caq	gct	gca	ccc	atq	gca	gaa	gga	96
137 Tyr Leu		-	-	-	_	_	-		_	-	_		
138	20		<u>.</u>		25					30		-4	
140 gga ggg			cac q	aa qto			tte	ato	gat			caq	144
141 Gly Gly													
4 4						_					_		

RAW SEQUENCE LISTING DATE: 06/12/2001 PATENT APPLICATION: US/09/297,486 TIME: 13:11:24

Input Set : A:\GJE-30.txt

Output Set: N:\CRF3\06122001\1297486.raw

144 cgc agc tac tgc cat cca atc gag acc ctg gtg gac atc ttc cag gag 145 Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu 146 50 55 60 158 acc tgat gag atc gas tac atc ttc aag cca tcc tgt gtg ccg ctg 149 Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu 150 65 70 75 80 152 atg cga tgc ggg ggc tgc tgc gaa gac gag ggc ctg gag tgt gtg ccc 153 Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro 154 85 90 95 156 act gag gag tcc ac ac atc acc atg cag att atg cgg atc aca acc acc atg 157 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His 158 100 105 110 160 caa ggc cag cac ata gag aga gag agc ttc cta cag cac aca aca act tgc 157 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His 158 100 105 110 160 caa ggc cag cac ata gga gag atg agc ttc cta cag cac aca aca act tgc 151 120 120 125 164 gaa tgc aga cca aag aaa gat aga gc ttc cta cag cac aca aca act tgc 165 Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Pro Cys Gly 166 130 135 140 168 cct tgc tca gag cgg aga aca act ttg ttg ta cac aga cac acc acc 173 Cys Lys Cys Ser Cys Lys Asn Thr Asp Ser Arg Cys Lys Ala Arg Gln 174 165 150 175 175 160 176 ctt gag tta acc gaa cgt act tgc aca acc acc acc acc 173 Cys Lys Cys Ser Cys Lys Asn Thr Asp Ser Arg Cys Lys Ala Arg Gln 174 165 170 175 175 180 180 180 180 180 180 180 180 180 180 180		142 35 40 45																	
146	142			35					40					45					
146	144	cgc	agc	tac	tgc	cat	cca	atc	gag	acc	ctg	gtg	gac	atc	ttc	cag	gag		192
146																			
149 Tyr Pro Asp Clu Ile Clu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu	146		50					55					60						
149 Tyr Pro Asp Clu Tie Clu Tyr Tie Phe Lys Pro Ser Cys Val Pro Leu 150 65 70 75 80 80 152 atg cga tgc ggg ggc tgc tgc aat gac gag ggc ctg gag tgt gtg ccc 288 153 Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro 156 80 90 95 91 160 1	148	tac	cct	gat	gag	atc	gag	tac	atc	ttc	aaq	cca	tcc	tgt	qtq	ccq	ctg		240
150 65 70 75 80											-			_		_	-		
153 Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro 154 85 90 95 95 156 act gag gag tcc aac atc acc atg cag att at atg cgg atc aaa cct cac 336 157 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His 158 100 105 110				-				•			-			_					
153 Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro 154 85 90 95 95 156 act gag gag tcc aac atc acc atg cag att at atg cgg atc aaa cct cac 336 157 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His 158 100 105 110	152	atq	cga	tqc	qqq	qqc	tqc	tqc	aat	qac	qaq	qqc	ctq	qaq	tat	ata	ccc		288
154																			
157 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His 158 100 105 110			-	•	-	_	-	-		*		-			-				
157 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His 158 100 105 110	156	act	gag	gag	tcc	aac	atc	acc	atq	caq	att	atq	cqq	atc	aaa	cct	cac		336
158																			
161 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys 115 120													_		_				
161 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys 115 120	160	caa	ggc	cag	cac	ata	qqa	qaq	atq	agc	ttc	cta	caq	cac	aac	aaa	tat		384
162																			
165 Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Pro Cys Gly 166			-				1									-1-	-1-		
165 Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Pro Cys Gly 166	164	qaa	tac	aσa	cca	aaσ	aaa	gat		σca	aga	caa	gaa		ccc	t.at.	aaa		432
166									-		-		-			_			
169 Pro Cys Ser Glu				3			-1-		5					-1-		- 1 -	1		
169 Pro Cys Ser Glu	168	cct	tac	tca	gag	caa	aga	aaσ	cat	tta	ttt	σta	caa	σat	cca	cag	acq		480
170 145																			
172 tgt aaa tgt tcc tgc aaa aac aca gac tcg cgt tgc aag gcg agg cag			•			,	-												
173 Cys Lys Cys Ser Cys Lys Asn Thr Asp Ser Arg Cys Lys Ala Arg Gln 174	•		aaa	tat	tcc	tac		aac	aca	gac	tca		tac	aaq	aca	agg			528
174																			
176 ctt gag tta aac gaa cgt act tgc aga tgt gac aag ccg agg cgg/ 177 Leu Glu Leu Asn Glu Arg Thr Cys Arg Cys Asp Lys Pro Arg Arg 178		-	-	1			1 -			1		,	-1-	-1-		_			
177 Leu Glu Leu Asn Glu Arg Thr Cys Arg Cys Asp Lys Pro Arg Arg 178	176	ctt	qaq	tta	aac	qaa	cat	act	tac	aga		gac	aaq	cca	agg		/		573
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184 <213> ORGANISM: Homo sapiens 186 <400> SEQUENCE: 4 188 Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu 189 1 5 10 15 191 Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly 192 20 25 30 194 Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln 195 35 40 45 197 Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu 198 50 55 60 200 Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu 201 65 70 75 80 203 Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro 204 85 90 95 206 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His 207 100 105 105 110 209 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys	183	<212	2> TY	PE:	PRT														
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192	189	1				5					10					15			
194 Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln 195	191	Tyr	Leu	His	His	Ala	Lys	Trp	Ser	Gln	Ala	Ala	Pro	Met	Ala	Glu	Gly	·	
195	192				20					25					30		_		
197 Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu 198 50	194	Gly	Gly	Gln	Asn	His	His	Glu	Val	Val	Lys	Phe	Met	Asp	Val	Tyr	Gln		
198	195			35					40					45					
200 Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu 201 65	197	Arg	Ser	Tyr	Cys	His	Pro	Ile	Glu	Thr	Leu	Val	Asp	Ile	Phe	Gln	Glu		
201 65 70 75 80 203 Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro 204 85 90 95 206 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His 207 100 105 110 209 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys	198		50					55					60						
203 Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro 204	200	Tyr	Pro	Asp	Glu	Ile	Glu	Tyr	Ile	Phe	Lys	Pro	Ser	Cys	Val	Pro	Leu		
204 85 90 95 206 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His 207 100 105 110 209 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys	201	65					70					75					80		
204 85 90 95 206 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His 207 100 105 110 209 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys	203	Met	Arg	Cys	Gly	Gly	Cys	Cys	Asn	Asp	Glu	Gly	Leu	Glu	Cys	Va:1	Pro		
207 100 105 110 209 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys					_					-		_			_				
207 100 105 110 209 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys	206	Thr	Glu	Glu	Ser	Asn	Ile	Thr	Met	Gln	Ile	Met	Arg	Ile	Lys	Pro	His		
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RAW SEQUENCE LISTING

DATE: 06/12/2001

PATENT APPLICATION: US/09/297,486

TIME: 13:11:24

Input Set : A:\GJE-30.txt
Output Set: N:\CRF3\06122001\I297486.raw

212 213	Glu	Cys 130	Arg	Pro	Lys	Lys	Asp 135	Arg	Ala	Arg	Gln	Glu 140	Lys	Pro	Cys	Gly	
	Pro 145	Cys	Ser	Glu	Arg	Arg 150	Lys	His	Leu	Phe	Val 155	Gln	Asp	Pro	Gln	Thr 160	
218		Lys	Cys	Ser	_	•	Asn	Thr	Asp			Cys	Lys	Ala	Arg		
219	Leu	Glu	Leu	Asn	165	Ara	Thr	Cvs	Ara	170 Cvs	Asp	Lvs	Pro	Ara	175 Arg		
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236	Met	Asn	Phe	Leu	Leu	Ser	Trp	Val	His	${\tt Trp}$	Ser	Leu	Ala	Leu	Leu	Leu	
237	1				5					10					15		
															gaa		96
	Tyr	Leu	His		Ala	Lys	Trp	Ser		Ala	Ala	Pro	Met		Glu	Gly	
241				20					25		++~	-+ <i>-</i> -	~-+	30	+ - +	~~~	1 4 4
															tat Tyr		144
245	СТУ	GIY	35	ASII	птъ	птэ	GIU	40	vai	цуз	FIIE	Mec	45	Val	тут	GIII	
	cac	age		tac	cat	сса	atc		acc	cta	ata	gac		ttc	cag	σασ	192
	_	_		_											Gln		
249		50	_1_	- 1			55					60					
251	tac	cct	gat	gag	atc	gag	tac	atc	ttc	aag	cca	tcc	tgt	gtg	ccg	ctg	240
252	Tyr	Pro	Asp	Glu	Ile	Glu	Tyr	Ile	Phe	Lys	Pro	Ser	Cys	Val	Pro	Leu	
253	65					70					75					80	
															gtg		288
	Met	Arg	Cys	Gly		Cys	Cys	Asn	Asp		Gly	Leu	Glu	Cys	Val	Pro	
257					85					90	~ * ~	~~~	- - '		95		. 226
															cct Pro		. 336
261	1111	GIU	GIU	100	ASII	116	1111	Mec	105	116	Mec	Alg	116	110	FIO	1113	
	caa	aac	caq		ata	gga	σασ	atσ		t.t.c	cta	caσ	cac		aaa	t.at.	384
															Lys		
													125		•	-	
													aaa	aaa	tca	gtt	432
268	Glu	Cys	Arg	Pro	Lys	Lys	Asp	Arg	Ala	Arg	Gln	Glu	Lys	Lys	Ser	Val	•
269		130					135					140					
															cgg		480
	_	Gly	Lys	Gly	Lys	_	Gln	Lys	Arg	Lys		Lys	Lys	Ser	Arg		
	145				-4	150			+	+~-	155		~~~		225	160	E20
															aag		528
276	гЛЯ	per.	ттр	ser.	vai 165	PLO	Cys	стй	PIO	170	ser.	GIU	AIG	мту	Lys 175	uis	
4//					T03					1/0					1,5		

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Input Set : A:\GJE-30.txt

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282	a a c	taa	cat	180	220	aca	agg	cad	185	gag	tta	aac	αаа		act	tac		624
												Asn						024
286		501	195	O _I D			**** 9	200	Lou	014			205	5		-1-		
	aga	tgt	gac	aag	ccg	agg	cgg	-										645
	-	_	-	_	_	ro Arg Arg												
290		210					215											
)> SI																
		l> LI			15													
		2> TY																
						omo sapiens												
)> SI				Cor	(II ren	Wa 1	шіс	Trn	Cor	LOU	λla	Lou	LOU	LOU		
300		ASII	Pne	Leu	Leu 5	ser	пр	val	птэ	10	ser	Leu	Ата	цец	15	neu		
		Len	Иiс	Hic	_	Lvc	Trn	Ser	Gln		Δla	Pro	Met	Ala		G1 v		
304	111	пси	HID	20	2114	1,5	111	JCI	25		1124	110	1100	30	014	011		
	Glv	Glv	Gln		His	His	Glu	Val		Lys	Phe	Met	Asp		Tyr	Gln		
307	1	1	35					40		_			45		-			
309	Arg	Ser	Tyr	Cys	His	Pro	Ile	Glu	Thr	Leu	Val	Asp	Ile	Phe	Gln	Glu		
310		50					55					60						
312	\mathtt{Tyr}	Pro	Asp	Glu	Ile	Glu	Tyr	Ile	Phe	Lys	Pro	Ser	Cys	Val	Pro			
313	65				_	70					75			_	3	80		
	Met	Arg	Cys	Gly		Cys	Cys	Asn	Asp		GLY	Leu	Glu	Cys		Pro		
316	m	a 1	G 2	a	85	т1.	m b so	Wa+	<i>c</i> 15	90	Mot	7 ~~	т10	Tura	95	ni c		
319	THE	GIU	GIU	100	ASII	TTE.	1111	мес	105	116	Met	Arg	116	110	PIO	птэ		
	Gln	Glv	Gln		Tle	Glv	Glu	Met		Phe	Leu	Gln	His		Lvs	Cvs		
322	0111		115	1110			014	120	001		200	0	125		-1-	-1-		
	Glu	Cys		Pro	Lys	Lys	Asp	Arg	Ala	Arg	Gln	Glu	Lys	Lys	Ser	Val		
325		130			-	-	135	-		_		140						
327	Arg	Gly	Lys	Gly	Lys	Gly	Gln	Lys	Arg	Lys	Arg	Lys	Lys	Ser	Arg	Tyr		
328						150					155					160		
	Lys	Ser	Trp	Ser		Pro	Cys	Gly	Pro	_	Ser	Glu	Arg	Arg		His		
331	_	_,	1	a 1	165	_	~ 1	m1		170	a	a	G	T	175	m la an		
	Leu	Pne	val		Asp	Pro	GIN	Thr	185	ьуs	Cys	Ser	Cys	LуS 190	ASII	THE		
334	λαρ	Cor	λνα	180	Twc	בוג	λνα	Gln		Glu	LAU	Asn	Glu		Thr	Cve		
337	АЗР	ser	195	Cys	пур	Ата		200		GIU	пец		205		1111	Cys		
	Ara	Cys		Lvs	Pro	Ara		200					200					
340	9	210		1-		5	215											
	3 <210> SEQ ID NO: 7																	
		L> LE																
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		3> OF			Homo	sap	oiens	5										
)> FE																
		> NA																
350	<222	2> LC	CAT1	LON:	16	96												

VERIFICATION SUMMARY

DATE: 06/12/2001

PATENT APPLICATION: US/09/297,486

TIME: 13:11:25

Input Set : A:\GJE-30.txt
Output Set: N:\CRF3\06122001\I297486.raw

L:14 M:271 C: Current Filing Date differs, Replaced Current Filing Date